VII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Li have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

March 1, 2004

Date

Lance K Ishimoto Reg. No. 41,866

LEXICON GENETICS INCORPORATED (281) 863-3333

Customer # 24231

Pathobiology. 1995;63(5):288-92.

Related Articles, Links

Lack of natural killer cell augmentation in vitro by human interferon gamma in a subset of patients with systemic sclerosis.

Wanchu A, Singh VK, Yadav VS, Biswas S, Misra R, Agarwal SS.

Department of Immunology, Sanjay Gandhi Post-Graduate Institute of Medical Sciences, Lucknow, India.

Systemic sclerosis (SSc) is a generalized connective tissue disorder characterized by fibrosis of skin and various viscera. Natural killer (NK) cells are a subset of lymphocytes that can lyse targets without prior sensitization. Few studies have tried to assess NK cell function in patients with SSc. To evaluate NK cell cytotoxicity in patients with SSc and to see the extent of its augmentation in vitro by human interferon (hIFN) gamma in the clinical subset of limited and diffuse cutaneous diseases, we evaluated 27 patients with SSc and 22 age- and sex-matched controls by 51Cr release assay. Fifteen patients had limited cutaneous disease (mean disease duration 6.2 +/- 2.7 years) and 12 diffuse cutaneous disease (mean disease duration 5.7 +/- 2.4 years). Patients with limited SSc had significantly higher baseline NK cell function than controls (p < 0.05) and the augmentation following in vitro stimulation with hIFN gamma was negligible. Patients with diffuse SSc had lower baseline NK cell cytotoxicity than controls but this was not statistically significant. Augmentation with hIFN gamma in this group was comparable to controls. This study suggests that NK cells may have a role in the pathophysiology of this disease.

PMID: 8724212 [PubMed - indexed for MEDLINE]

J Investig Allergol Clin Immunol. 2003;13(2):87-93.

Related Articles, Links

Analysis of lymphocyte subpopulations in systemic sclerosis.

Ercole LP, Malvezzi M, Boaretti AC, Utiyama SR, Rachid A.

Department of Medicine, Hospital de Clinicas of the Federal University of Parana, Curitiba, Parana, Brazil.

Systemic sclerosis (SSc) is a chronic inflammatory connective-tissue disease of unknown etiology, characterized by fibrosis and microvascular injury in affected organs. It has become · clear that the activated cellular-immune system plays a central role in the pathogenesis of SSc. This study analyzes the numbers of lymphocyte subpopulations and their relations with clinical and laboratory manifestations. We studied a group of 42 patients with SSc and a group of 28 matched normal controls by flow cytometry using the lymphocyte cell-surface markers CD2, CD3, CD4, CD8, CD19, CD25, CD45RA, CD56, CD71, HLA-DR, TCR alpha/beta, and TCR gamma/delta. Patients with SSc had similar percentages of CD2+, CD3+, CD3+, CD3+, CD3+, CD8+, CD25+, CD4+ CD45RA+, CD8+ CD45RA+, CD71+ cells, and CD4+/CD8+ cell ratio when compared to normal controls. In contrast, the percentages of TCR gamma/delta cells were significantly lower in SSc patients with diffuse and late-stage disease with pulmonary involvement, muscle involvement, and the presence of anti-Scl-70 antibodies. Patients with diffuse SSc in early- and late-stage disease had significantly increased percentages of HLA-DR in CD4+ and CD8+ cells. Patients with late-stage disease had increased percentages of CD4+ CD45RA+ T-cells. Patients with limited and early-stage disease had smaller percentages of Bcells (CD19+). Patients with diffuse and late-stage disease had smaller percentages of NK-cells (CD56+). These results suggest that T-, B-, and NK-cell alterations may be involved in the onset of the disease, and/or in the perpetuation of disease, and may eventually be useful as a prognostic indicator in selected patient subgroups.

PMID: 12968391 [PubMed - in process]